Guidelines for the Use of Antiretroviral Agents in Pediatric HIV Infection

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Table 17f. Antiretroviral Therapy-Associated Adverse Effects and Management Recommendations—Insulin Resistance, Asymptomatic Hyperglycemia, Diabetes Mellitus (Last updated November 1, 2012; last reviewed November 1, 2012)

Adverse Effects	Associated ARVs	Onset/Clinical Manifestations	Estimated Frequency	Risk Factors	Prevention / Monitoring	Management
Insulin resistance, asymptomatic hyperglycemia, DM[a]	Thymidine analogue NRTIs (d4T, ddI, ZDV) Some PIs (IDV, LPV/r; perhaps less often ATV, ATV/r, DRV/r, TPV/r)	Onset: Weeks to months after beginning therapy; median of 60 days (adult data) Presentation: *Most commonly:* Asymptomatic fasting hyperglycemia (possibly in the setting of lipodystrophy), metabolic syndrome, or growth delay *Also possible:* Frank DM (polyuria, polydipsia, polyphagia, fatigue, hyperglycemia)	Impaired fasting glucose: *ARV-treated adults:* 3%–25% *ARV-treated children:* 0%–7% Impaired glucose tolerance: *ARV-treated adults:* 16%–35% *ARV-treated children:* 3%–4% DM: *ARV-treated adults:* 0.6–4.7 per 100 person-years (2- to 4-fold greater than that for HIV-uninfected adults) *ARV-treated children:* Very rare in HIV-infected children	Risk factors for Type 2 DM: Lipodystrophy Metabolic syndrome Family history of DM High BMI Obesity	Prevention: Lifestyle modification (see Management). Although uncertain, avoiding use of d4T, IDV may reduce risk. Monitoring: Monitor for polydipsia, polyuria, polyphagia, change in body habitus, acanthosis nigricans. *Obtain RPG levels at*: Initiation of ARV therapy; 3–6 months after therapy initiation; and once a year thereafter. For RPG ≥140 mg/dL, obtain FPG performed after 8-hour fast and consider referral to endocrinologist.	Counsel on lifestyle modification (low-fat diet, exercise, no smoking). Consider changing from thymidine analogue NRTI (d4T or ZDV)-containing regimen. *For either RPG ≥200 mg/dL plus symptoms of DM or FPG ≥126 mg/dL:* Patient meets diagnostic criteria for DM; consult endocrinologist. *FPG 100–125 mg/dL:* Impaired FPG is suggestive of insulin resistance; consult endocrinologist. *FPG <100 mg/dL:* Normal FPG but does not exclude insulin resistance; recheck FPG in 6–12 months.

[a] Insulin resistance, asymptomatic hyperglycemia, and DM form a spectrum of increasing severity. *Insulin resistance* is often defined as elevated insulin levels for the level of glucose observed; *impaired FPG* as an FPG of 100–125 mg/dL; *impaired glucose tolerance* as an elevated 2-hour PG of 140–199 mg/dL in a standard OGTT; and *diabetes mellitus* as either an FPG ≥126 mg/dL, a random PG ≥200 mg/dL in a patient with hyperglycemia symptoms, an HgbA1C of ≥6.5%, or a 2-hour PG after OGTT ≥200 mg/dL. However, the Panel does not recommend routine determinations of insulin levels, HgbA1C, or glucose tolerance without consultation with an endocrinologist; these guidelines are instead based on the readily available random and fasting plasma glucose levels.

Key to Acronyms: ARV = antiretroviral, ATV = atazanavir, ATV/r = atazanavir/ritonavir, d4T = stavudine, ddI = didanosine, DM = diabetes mellitus, DRV/r = darunavir/ritonavir, FPG = fasting plasma glucose, IDV = indinavir, LPV/r = lopinavir/ritonavir, NRTI = nucleoside reverse transcriptase inhibitor, OGTT = oral glucose tolerance test, PG = plasma glucose, PI = protease inhibitor, RPG = random plasma glucose, TPV/r = tipranavir/ritonavir, ZDV = zidovudine

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